

SEQUENCE LISTING

<110> Philip E. Thorpe
Rolf A. Brekken

<120> ANTIBODY CONJUGATE METHODS FOR SELECTIVELY INHIBITING VEGF

<130> 4001.002585

<140> UNKNOWN

<141> 2000-04-28

<150> 60/131,432

<151> 1999-04-28

<160> 44

<170> PatentIn Ver. 2.0

<210> 1

<211> 2149

<212> DNA

<213> Homo sapiens

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<212> PRT
<213> Homo sapiens

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35 40 45
Glu His Asp Gly Asn Cys Arg Glu Ser Thr Thr Asp Gln Tyr Asn Thr
50 55 60
Asn Ala Leu Gln Arg Asp Ala Pro His Val Glu Pro Asp Phe Ser Ser
65 70 75 80
Gln Lys Leu Gln His Leu Glu His Val Met Glu Asn Tyr Thr Gln Trp
85 90 95
Leu Gln Lys Leu Glu Asn Tyr Ile Val Glu Asn Met Lys Ser Glu Met
100 105 110
Ala Gln Ile Gln Gln Asn Ala Val Gln Asn His Thr Ala Thr Met Leu
115 120 125
Glu Ile Gly Thr Ser Leu Leu Ser Gln Thr Ala Glu Gln Thr Arg Lys
130 135 140
Leu Thr Asp Val Glu Thr Gln Val Leu Asn Gln Thr Ser Arg Leu Glu
145 150 155 160
Ile Gln Leu Leu Glu Asn Ser Leu Ser Thr Tyr Lys Leu Glu Lys Gln
165 170 175
Leu Leu Gln Gln Thr Asn Glu Ile Leu Lys Ile His Glu Lys Asn Ser
180 185 190
Leu Leu Glu His Lys Ile Leu Glu Met Glu Gly Lys His Lys Glu Glu
195 200 205
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210 215 220
Arg Gln Thr Tyr Ile Ile Gln Glu Leu Glu Lys Gln Leu Asn Arg Ala
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 325 330 335
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 Tyr Arg Leu Tyr Leu Lys Gly His Thr Gly Thr Ala Gly Lys Gln Ser
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 435 440 445
 Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Phe Tyr Thr Ala
 450 455 460
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<210> 3
 <211> 2269
 <212> DNA
 <213> Homo sapiens

<400> 3

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<210> 4

<211> 496

<212> PRT

<213> Homo sapiens

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<400> 4

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20

25

30

Gln Tyr Gln Val Gln His Gly Ser Cys Ser Tyr Thr Phe Leu Leu Pro

35

40

45

Glu Met Asp Asn Cys Arg Ser Ser Ser Pro Tyr Val Ser Asn Ala

50	55	60	
Val Gln Arg Asp Ala Pro	Leu Glu Tyr Asp Asp	Ser Val Gln Arg Leu	
65	70	75	80
Gln Val Leu Glu Asn Ile	Met Glu Asn Asn Thr	Gln Trp Leu Met Lys	
85	90	95	
Leu Glu Asn Tyr Ile Gln Asp Asn Met Lys	Lys Glu Met Val Glu Ile		
100	105	110	
Gln Gln Asn Ala Val Gln Asn Gln Thr Ala Val Met Ile	Glu Ile Gly		
115	120	125	
Thr Asn Leu Leu Asn Gln Thr Ala Glu Gln Thr Arg	Lys Leu Thr Asp		
130	135	140	
Val Glu Ala Gln Val Leu Asn Gln Thr Thr Arg	Leu Glu Leu Gln Leu		
145	150	155	160
Leu Glu His Ser Leu Ser Thr Asn Lys	Leu Glu Lys Gln Ile Leu Asp		
165	170	175	
Gln Thr Ser Glu Ile Asn Lys	Leu Gln Asp Lys Asn Ser Phe Leu Glu		
180	185	190	
Lys Lys Val Leu Ala Met Glu Asp	Lys His Ile Ile Gln Leu Gln Ser		
195	200	205	
Ile Lys Glu Glu Lys Asp	Gln Leu Gln Val Leu Val Ser Lys Gln Asn		
210	215	220	
Ser Ile Ile Glu Glu Leu Glu Lys	Ile Val Thr Ala Thr Val Asn		
225	230	235	240
Asn Ser Val Leu Gln Lys	Gln Gln His Asp Leu Met Glu Thr Val Asn		
245	250	255	
Asn Leu Leu Thr Met Met Ser	Thr Ser Asn Ser Ala Lys Asp Pro Thr		
260	265	270	
Val Ala Lys Glu Glu Gln Ile	Ser Phe Arg Asp Cys Ala Glu Val Phe		
275	280	285	
Lys Ser Gly His Thr Thr Asn Gly	Ile Tyr Thr Leu Thr Phe Pro Asn		
290	295	300	
Ser Thr Glu Glu Ile Lys	Ala Tyr Cys Asp Met Glu Ala Gly Gly		
305	310	315	320
Gly Trp Thr Ile Ile Gln Arg Arg	Glu Asp Gly Ser Val Asp Phe Gln		
325	330	335	
Arg Thr Trp Lys Glu Tyr Lys Val	Gly Phe Gly Asn Pro Ser Gly Glu		
340	345	350	
Tyr Trp Leu Gly Asn Glu Phe Val	Ser Gln Leu Thr Asn Gln Arg		

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Tyr Val Leu Lys Ile His Leu Lys Asp Trp Glu Gly Asn Glu Ala Tyr		
370	375	380
Ser Leu Tyr Glu His Phe Tyr Leu Ser Ser Glu Glu Leu Asn Tyr Arg		
385	390	395
Ile His Leu Lys Gly Leu Thr Gly Thr Ala Gly Lys Ile Ser Ser Ile		
405	410	415
Ser Gln Pro Gly Asn Asp Phe Ser Thr Lys Asp Gly Asp Asn Asp Lys		
420	425	430
Cys Ile Cys Lys Cys Ser Gln Met Leu Thr Gly Gly Trp Trp Phe Asp		
435	440	445
Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Tyr Tyr Pro Gln Arg Gln		
450	455	460
Asn Thr Asn Lys Phe Asn Gly Ile Lys Trp Tyr Trp Lys Gly Ser		
465	470	475
Gly Tyr Ser Leu Lys Ala Thr Thr Met Met Ile Arg Pro Ala Asp Phe		
485	490	495
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<212> PRT		
<213> Homo sapiens		
<400> 5		
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20	25	30
Gln Tyr Gln Val Gln His Gly Ser Cys Ser Tyr Thr Phe Leu Leu Pro		
35	40	45
Glu Met Asp Asn Cys Arg Ser Ser Ser Pro Tyr Val Ser Asn Ala		
50	55	60
Val Gln Arg Asp Ala Pro Leu Glu Tyr Asp Phe Ser Ser Gln Lys Leu		
65	70	75
80		
Gln His Leu Glu His Val Met Glu Asn Tyr Thr Gln Trp Leu Gln Lys		
85	90	95
Leu Glu Asn Tyr Ile Val Glu Asn Met Lys Ser Glu Met Ala Gln Ile		
100	105	110
Gln Gln Asn Ala Val Gln Asn His Thr Ala Thr Met Leu Glu Ile Gly		
115	120	125

Thr Ser Leu Leu Ser Gln Thr Ala Glu Gln Thr Arg Lys Leu Thr Asp
 130 135 140

Val Glu Thr Gln Val Leu Asn Gln Thr Ser Arg Leu Glu Ile Gln Leu
 145 150 155 160

Leu Glu Asn Ser Leu Ser Thr Tyr Lys Leu Glu Lys Gln Leu Leu Gln
 165 170 175

Gln Thr Asn Glu Ile Leu Lys Ile His Glu Lys Asn Ser Leu Leu Glu
 180 185 190

His Lys Ile Leu Glu Met Glu Gly Lys His Lys Glu Glu Leu Asp Thr
 195 200 205

Leu Lys Glu Glu Lys Glu Asn Leu Gln Gly Leu Val Thr Arg Gln Thr
 210 215 220

Tyr Ile Ile Gln Glu Leu Glu Lys Gln Leu Asn Arg Ala Thr Thr Asn
 225 230 235 240

Asn Ser Val Leu Gln Lys Gln Leu Glu Leu Met Asp Thr Val His
 245 250 255

Asn Leu Val Asn Leu Ser Thr Lys Glu Gly Val Leu Leu Lys Gly Gly
 260 265 270

Lys Arg Glu Glu Lys Pro Phe Arg Asp Cys Ala Asp Val Tyr Gln
 275 280 285

Ala Gly Phe Asn Lys Ser Gly Ile Tyr Thr Ile Tyr Ile Asn Asn Met
 290 295 300

Pro Glu Pro Lys Lys Val Phe Cys Asn Met Asp Val Asn Gly Gly
 305 310 315 320

Trp Thr Val Ile Gln His Arg Glu Asp Gly Ser Leu Asp Phe Gln Arg
 325 330 335

Gly Trp Lys Glu Tyr Lys Met Gly Phe Gly Asn Pro Ser Gly Glu Tyr
 340 345 350

Trp Leu Gly Asn Glu Phe Ile Phe Ala Ile Thr Ser Gln Arg Gln Tyr
 355 360 365

Met Leu Arg Ile Glu Leu Met Asp Trp Glu Gly Asn Arg Ala Tyr Ser
 370 375 380

Gln Tyr Asp Arg Phe His Ile Gly Asn Glu Lys Gln Asn Tyr Arg Leu
 385 390 395 400

Tyr Leu Lys Gly His Thr Gly Thr Ala Gly Lys Gln Ser Ser Leu Ile
 405 410 415

Leu His Gly Ala Asp Phe Ser Thr Lys Asp Ala Asp Asn Asn Cys
 420 425 430

Met Cys Lys Cys Ala Leu Met Leu Thr Gly Gly Trp Trp Phe Asp Ala
435 440 445

Cys Gly Pro Ser Asn Leu Asn Gly Met Phe Tyr Thr Ala Gly Gln Asn
450 455 460

His Gly Lys Leu Asn Gly Ile Lys Trp His Tyr Phe Lys Gly Pro Ser
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<210> 6

<211> 381

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: SYNTHETIC
OLIGONUCLEOTIDE

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<210> 7

<211> 127

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

<400> 7

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20 25 30

Ser Tyr Val Phe His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Asn Pro Tyr Asn Asp Val Thr Lys Tyr Asn Glu
50 55 60

Lys Phe Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr
65 70 75 80

Ala Tyr Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr
85 90 95

Tyr Cys Ala Ser Tyr Tyr Gly Ser Ser Tyr Gly Tyr Tyr Ala Met Asp
100 105 110

Asp Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly
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<210> 8

<211> 347

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: SYNTHETIC
OLIGONUCLEOTIDE

<400> 8

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gaatctgggg tccctgatcg cttcacagggc agtggatctg gaaccgattt cactcttacc 240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
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<210> 9

<211> 115

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

<400> 9

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Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile His Gly Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu

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105

110

Lys Arg Leu
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<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

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1 5 10 15

Phe Met Asp Val Tyr Gln Arg Ser Tyr Cys
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<210> 11
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

<400> 11
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Met Asp Val Tyr Lys Arg Ser Tyr Cys
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<210> 12
<211> 573
<212> DNA
<213> Artificial Sequence

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<223> Description of Artificial Sequence: SYNTHETIC
OLIGONUCLEOTIDE

<220>
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Leu His Leu Val Ala Leu Asn Thr Pro Leu Ser Gly Gly Met Arg Gly	
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Ile Arg Gly Ala Asp Phe Gln Cys Phe Gln Gln Ala Arg Ala Val Gly	
35 40 45	
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Leu Ser Gly Thr Phe Arg Ala Phe Leu Ser Ser Arg Leu Gln Asp Leu	
50 55 60	
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Tyr Ser Ile Val Arg Arg Ala Asp Arg Gly Ser Val Pro Ile Val Asn	
65 70 75 80	
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Leu Lys Asp Glu Val Leu Ser Pro Ser Trp Asp Ser Leu Phe Ser Gly	
85 90 95	
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Ser Gln Gly Gln Leu Gln Pro Gly Ala Arg Ile Phe Ser Phe Asp Gly	
100 105 110	
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Arg Asp Val Leu Arg His Pro Ala Trp Pro Gln Lys Ser Val Trp His	
115 120 125	
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Gly Ser Asp Pro Ser Gly Arg Arg Leu Met Glu Ser Tyr Cys Glu Thr	
130 135 140	
tgg cga act gaa act act ggg gct aca ggt cag gcc tcc tcc ctg ctg	480
Trp Arg Thr Glu Thr Thr Gly Ala Thr Gly Gln Ala Ser Ser Leu Leu	
145 150 155 160	
tca ggc agg ctc ctg gaa cag aaa gct gcg agc tgc cac aac agc tac	528
Ser Gly Arg Leu Leu Glu Gln Lys Ala Ala Ser Cys His Asn Ser Tyr	
165 170 175	
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Ile Val Leu Cys Ile Glu Asn Ser Phe Met Thr Ser Phe Ser Lys	
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<210> 13
 <211> 191
 <212> PRT
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 <223> Description of Artificial Sequence: SYNTHETIC
 PEPTIDE

<400> 13
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 1 5 10 15

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 20 25 30
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 35 40 45
 Leu Ser Gly Thr Phe Arg Ala Phe Leu Ser Ser Arg Leu Gln Asp Leu
 50 55 60
 Tyr Ser Ile Val Arg Arg Ala Asp Arg Gly Ser Val Pro Ile Val Asn
 65 70 75 80
 Leu Lys Asp Glu Val Leu Ser Pro Ser Trp Asp Ser Leu Phe Ser Gly
 85 90 95
 Ser Gln Gly Gln Leu Gln Pro Gly Ala Arg Ile Phe Ser Phe Asp Gly
 100 105 110
 Arg Asp Val Leu Arg His Pro Ala Trp Pro Gln Lys Ser Val Trp His
 115 120 125
 Gly Ser Asp Pro Ser Gly Arg Arg Leu Met Glu Ser Tyr Cys Glu Thr
 130 135 140
 Trp Arg Thr Glu Thr Thr Gly Ala Thr Gly Gln Ala Ser Ser Leu Leu
 145 150 155 160
 Ser Gly Arg Leu Leu Glu Gln Lys Ala Ala Ser Cys His Asn Ser Tyr
 165 170 175
 Ile Val Leu Cys Ile Glu Asn Ser Phe Met Thr Ser Phe Ser Lys
 180 185 190

<210> 14
 <211> 182
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 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: SYNTHETIC
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<400> 14
 His Ser His Arg Asp Phe Gln Pro Val Leu His Leu Val Ala Leu Asn
 1 5 10 15
 Ser Pro Leu Ser Gly Gly Met Arg Gly Ile Arg Gly Ala Asp Phe Gln
 20 25 30
 Cys Phe Gln Gln Ala Arg Ala Val Gly Leu Ala Gly Thr Phe Arg Ala
 35 40 45
 Phe Leu Ser Ser Arg Leu Gln Asp Leu Tyr Ser Ile Val Arg Arg Ala
 50 55 60

Asp	Arg	Ala	Ala	Val	Pro	Ile	Val	Asn	Leu	Lys	Asp	Glu	Leu	Leu	Phe
65															80
Pro	Ser	Trp	Glu	Ala	Leu	Phe	Ser	Gly	Ser	Glu	Gly	Pro	Leu	Lys	Pro
		85						90							95
Gly	Ala	Arg	Ile	Phe	Ser	Phe	Asp	Gly	Lys	Asp	Val	Leu	Arg	His	Pro
			100					105						110	
Thr	Trp	Pro	Gln	Lys	Ser	Val	Trp	His	Gly	Ser	Asp	Pro	Asn	Gly	Arg
		115					120							125	
Arg	Leu	Thr	Glu	Ser	Tyr	Cys	Glu	Thr	Trp	Arg	Thr	Glu	Ala	Pro	Ser
	130				135					140					
Ala	Thr	Gly	Gln	Ala	Ser	Ser	Leu	Leu	Gly	Gly	Arg	Leu	Leu	Gly	Gln
	145				150				155						160
Ser	Ala	Ala	Ser	Cys	His	His	Ala	Tyr	Ile	Val	Leu	Cys	Ile	Glu	Asn
				165					170						175
Ser	Phe	Met	Thr	Ala	Ser										
		180													

<210> 15

<211> 8

<212> PRT

<213> Artificial Sequence

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PEPTIDE

<400> 15

Pro	Arg	Phe	Lys	Ile	Ile	Gly	Gly
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<210> 16

<211> 8

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PEPTIDE

<400> 16

Pro	Arg	Phe	Arg	Ile	Ile	Gly	Gly
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<210> 17

<211> 9

<212> PRT

<213> Artificial Sequence

<220>
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PEPTIDE

<400> 17
Ser Ser Arg His Arg Arg Ala Leu Asp
1 5

<210> 18
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

<400> 18
Arg Lys Ser Ser Ile Ile Ile Arg Met Arg Asp Val Val Leu
1 5 10

<210> 19
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

<400> 19
Ser Ser Ser Phe Asp Lys Gly Lys Tyr Lys Lys Gly Asp Asp Ala
1 5 10 15

<210> 20
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

<400> 20
Ser Ser Ser Phe Asp Lys Gly Lys Tyr Lys Arg Gly Asp Asp Ala
1 5 10 15

<210> 21
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

<400> 21
Ile Glu Gly Arg
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<210> 22
<211> 4
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<220>
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PEPTIDE

<400> 22
Ile Asp Gly Arg
1

<210> 23
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<220>
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PEPTIDE

<400> 23
Gly Gly Ser Ile Asp Gly Arg
1 5

<210> 24
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
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PEPTIDE

<400> 24
Pro Leu Gly Leu Trp Ala
1 5

<210> 25
<211> 8
<212> PRT
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<220>

<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

<400> 25
Gly Pro Gln Gly Ile Ala Gly Gln
1 5

<210> 26
<211> 8
<212> PRT
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<220>
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PEPTIDE

<400> 26
Gly Pro Gln Gly Leu Leu Gly Ala
1 5

<210> 27
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

<400> 27
Gly Ile Ala Gly Gln
1 5

<210> 28
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: SYNTHETIC
PEPTIDE

<400> 28
Gly Pro Leu Gly Ile Ala Gly Ile
1 5

<210> 29
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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PEPTIDE

<400> 29
Gly Pro Glu Gly Leu Arg Val Gly
1 5

<210> 30
<211> 8
<212> PRT
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<220>
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PEPTIDE

<400> 30
Tyr Gly Ala Gly Leu Gly Val Val
1 5

<210> 31
<211> 8
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<220>
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PEPTIDE

<400> 31
Ala Gly Leu Gly Val Val Glu Arg
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<210> 32
<211> 8
<212> PRT
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PEPTIDE

<400> 32
Ala Gly Leu Gly Ile Ser Ser Thr
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<210> 33
<211> 8
<212> PRT
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<220>
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PEPTIDE

<400> 33
Glu Pro Gln Ala Leu Ala Met Ser
1 5

<210> 34
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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PEPTIDE

<400> 34
Gln Ala Leu Ala Met Ser Ala Ile
1 5

<210> 35
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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PEPTIDE

<400> 35
Ala Ala Tyr His Leu Val Ser Gln
1 5

<210> 36
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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PEPTIDE

<400> 36
Met Asp Ala Phe Leu Glu Ser Ser
1 5

<210> 37
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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PEPTIDE

<400> 37
Glu Ser Leu Pro Val Val Ala Val
1 5

<210> 38
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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PEPTIDE

<400> 38
Ser Ala Pro Ala Val Glu Ser Glu
1 5

<210> 39
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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PEPTIDE

<400> 39
Asp Val Ala Gln Phe Val Leu Thr
1 5

<210> 40
<211> 8
<212> PRT
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<220>
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PEPTIDE

<400> 40
Val Ala Gln Phe Val Leu Thr Glu
1 5

<210> 41
<211> 8
<212> PRT
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<220>
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PEPTIDE

<400> 41

Ala Gln Phe Val Leu Thr Glu Gly
1 5

<210> 42
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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PEPTIDE

<400> 42
Pro Val Gln Pro Ile Gly Pro Gln
1 5

<210> 43
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
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OLIGONUCLEOTIDE

<400> 43
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31

<210> 44
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: SYNTHETIC
OLIGONUCLEOTIDE

<400> 44
ctaccatggc tattggaga aagaggta

29